



16/Reply Brief  
02-17-93  
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PATENT  
1173-145P

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Teizo Yoshimura et al  
Serial No.: 07/330,446 Group: 1814  
Filed : March 30, 1989 Examiner: Dian Cook  
For : HUMAN DERIVED MONOCYTE ATTRACTING PURIFIED PROTEIN  
PRODUCT USEFUL IN A METHOD OF TREATING INFECTION AND  
NEOPLASMS IN A HUMAN BODY, AND THE CLONING OF FULL  
LENGTH cDNA THEREOF

REPLY BRIEF UNDER 37 C.F.R. 1.193(b)

Honorable Commissioner of Patents  
and Trademarks  
Washington, D.C. 20231

February 11, 1993

Sir:

In response to the Examiner's Answer dated January 11, 1993, to the Appellants' Brief on appeal filed October 13, 1992, the following remarks are provided for proper consideration by the Examiner and the Honorable Board of Patent Appeals and Interferences.

R E M A R K S

In the Examiner's Answer dated January 11, 1993, which was received in the matter of the above-identified application, new points of arguments were raised by the Examiner asserting that the Appellants' claims were unpatentable, and moreover that for purposes of the present Appeal they must stand or fall together.

Accordingly, based upon the provisions of 37 C.F.R. 1.193(b), the Appellants direct the following comments against such new points of argument raised by the Examiner in her Examiner's Answer dated January 11, 1993.

At page 3 of the Examiner's Answer, under the heading "Grouping of Claims" the Examiner asserts a new point of argument that Appellants' claims stand or fall together for purposes of the present Appeal. Specifically, the Examiner indicates as follows:

"Claims 11-19 depend upon claim 9, which is drawn to the cDNA encoding a monocyte chemo-attractant peptide. If said nucleotide sequence is patentable, then vectors, host cells, and methods of use are patentable also. On the contrary, if the cDNA is not found to be patentable, then claims in which the patentable feature is the DNA of interest are also not patentable. In other words, if the nucleic acid is not deemed to be patentable, then claims drawn to commonly used factors and host cells containing said DNA and method for use thereof to produce the protein encoded by said DNA are not patentable."

It is submitted to the Honorable Board Members that the above statement of the Examiner is without foundation. Specifically, the Examiner has provided no citation of appropriate authority to support her position.

Moreover, the Examiner's position is inappropriate, since the cDNA recited in claim 9 is a eukaryotic protein, while the expression system required in claims 13-19 is a prokaryotic expression system. Accordingly, since it is known by those skilled in the art that problems often arise in obtaining a biologically active eukaryotic protein, like that of claim 11, in prokaryotic

expression systems. For example, differences in post translational modifications between eukaryotic and prokaryotic cells can account for such difficulties.

Based upon such considerations, the Examiner's argument that the claims under appeal (claims 9 and 11-19) stand or fall together for purposes of the present appeal is not well taken, and the Honorable Board Members are respectfully requested to disregard such arguments. Instead, the Honorable Board is respectfully requested to consider the patentability of each of claims 9 and 11-19 separately, as indicated by the Appellants in their Appeal Brief (filed on October 13, 1992) at pages 4-5 thereof.

At pages 7-8 of the Examiner's Answer under the heading "Response to Argument" the Examiner has presented a fallacious new point of argument to rebut Appellants' assertion that the protein described by Valente is different from the chemotactic factor that is the subject of the claims. In particular the Examiner states,

The minimal molecular mass of appellants' proteins, based upon amino acid composition (which is different from the SDS-PAGE method used above), was 8400 Da. Appellants' assertion that the Valente et al peptide is distinct from the peptides disclosed by the present application based on molecular weight, is in essence, a comparison of apples to oranges. Appellants argue that their protein is distinct based upon one method of measurement, when in fact the specification teaches that using the same method of measurement as Valente et al, the proteins are the same weight.

Appellants do not dispute that two different methods are used to ascertain the molecular weight of the claimed factor and the

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protein purified by Valente et al. However, the Examiner is mistaken in alleging that the method used to determine the molecular weight of the claimed factor is amino acid composition. In fact, the molecular weight of the claimed factor is based upon determination of the amino acid sequence of the polypeptide by Edman degradation, i.e. solving the primary structure of the polypeptide. Thus, the 8400 Da molecular weight that was found is not a minimum weight based upon amino acid composition, but the true molecular weight of the protein.

Yoshimura  
p. 1959  
↓

The Examiner might choose to argue that the mass of the claimed protein was found to be approximately 15,000 Da when measured by SDS-PAGE, and in fact this may be true. However, Appellants assert that even if true, this fact would have little bearing on the present situation. Appellants noted the discrepancy in the molecular weight obtained and tried to find an explanation of the phenomenon by evaluating post-translational modification of the protein. No modifications of the protein that could explain the anomalous migration on SDS-PAGE gels was found (page 38, lines 7-17 of the Specification). Appellants emphasize that the Specification describes two factors which have chemotactic activity. GDCF-1, isolated from glioma cells and apparently identical to LDCF-1 which was isolated from leukocytes and has a molecular weight of 15,000 on SDS-PAGE gels. GDCF-2, also isolated from glioma cells and apparently identical to its leukocyte

counterpart LDCF-2 has a molecular weight of 13,000 by SDS-PAGE analysis.

It is the GDCF-2 protein which is the subject of the appealed claims. The Board of Patent Appeals and Interferences is requested to consider first that upon measurement by SDS-PAGE, the claimed polypeptide has a molecular weight of only 13,000 Da, compared to the 15,000 Da molecular weight observed for the protein isolated by Valente (an "apples to apples" comparison) and furthermore has a molecular weight of only 8400 as measured by determining the structure of the compound. Appellants therefore submit that the claimed GDCF-2 protein is distinct and unobvious from the protein described by Valente et al.

The Examiner may wish to argue that the difference between 13,000 Da and 15,000 Da is within the experimental error of electrophoretic measurement and argue that a "side-by-side" comparison of molecular weights must be performed. Appellants would therefore remind the Honorable Board Members that two chemotactic factors of similar molecular weight are described by the present application. Accordingly, if the Examiner alleges that the difference in molecular weight is in fact an experimental error, then she is implying that the protein isolated by Valente et al might in fact contain two distinguishable polypeptides. Accordingly, the Appellants submit that it would not be obvious from the disclosure of Valente et al which of the two proteins

would possess chemotactic activity and thus it cannot follow that the isolation of a single protein which in fact has chemo-attractant activity would be obvious under 35 U.S.C. §103 over the Valente disclosure.

C O N C L U S I O N

In consequence to the above remarks, the Honorable Board is again respectfully requested to reverse the Examiner's outstanding rejections of the claims, and to render a decision favorable to the Appellants in the matter of the above-identified application.

Please charge any fees or credit any overpayment pursuant to 37 C.F.R. 1.16 or 1.17 to Deposit Account Number 02-2448.

Respectfully submitted,

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